UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

MEMORANDUM:

From: Kevin Sweeney, Senior Entomologist

Date: September 5, 2014

Subject: PRODUCT PERFORMANCE DATA EVALUATION RECORD

This is a primary review. A contractor review was not performed.

DP barcode: 421168
Decision no.: 490010
Submission no: 950708
Action code: R340
Product Name: ThermaCELL Mosquito Repellent
EPA Reg. No: 71910-2
Formulation Type: RTU repellent mat
Ingredients statement from the label with PC codes included: 21.97% allethrin
Application rate(s) of product(s): 1 mat per 225 square feet (15 feet x 15 feet area)
Use Pattern: outdoor spatial repellent. Mat is heated with product device to release the active ingredient.
OCSPP Guidelines 810.3500 to the extent that it applies.

I. **Action Requested:** Review a new product performance field study (based on an EPA approved protocol) that provides data to support a 12 hour spatial repellency claim against mosquitoes.

II. **Background**: The registrant proposed a larger mat for this product that is twice the weight of the current mat. The registrant conducted a study to increase the repellency time on the product from 4 to 12 hours. The study was also submitted to support the claim "Repels mosquitoes from a 225 square feet (15 feet x 15 feet) area". The study included testing with the 4 hour (smaller mat) and the 12 hour (larger mat) against free flying and caged mosquitoes.

III. **Study Review**:

MRID49357001. Carroll, S. P. 2013. Field Evaluation of the Control and Repellent Efficacy of a Heated d-Allethrin Mat against Caged Mosquitoes. Carroll-Loye Biological Research, Davis, CA USA. 264 pp.

This study was conducted according to GLP.

Purpose: to evaluate this product under typical conditions against adult mosquitoes. The ability of the product to repel free flying mosquitoes was measured together with knockdown effects against caged mosquitoes.

Materials and Methods:

Protocol References:

- Carroll-Loye protocol ID number and title: SCI-005, 'Field Test Evaluation of the Control and Repellent Activity of a Heated d-Allethrin Mat to Caged and Free-flying Mosquitoes.'
- EPA review date for protocol: 11 July 2013
- Deviations from the protocol and their consequences are documented in Appendix 1.

Test Materials: the experiment tested the ThermaCELL 12 hour mat and the ThermaCELL 4 hour mat, each containing 21.7% (w/w) allethrin. The untreated control consisted of mats that contained no active or inert ingredients. The ThermaCELL emitter operated according to label instructions was used to heat the mats and vaporize the allethrin.

Laboratory reared mosquito species for knockdown evaluation in field cages (nylon mesh bags): adult *Aedes aegypti*, *Anopheles quadrimaculatus*, and *Culex quinquefasciatus*. There were 5 individuals per bag.

Carbon dioxide baited traps: these traps served as surrogate hosts and were used to lure mosquitoes into the treated and untreated areas.

Wild mosquitoes: these were monitored and captured using carbon dioxide baited traps. Results are presented in Table 7 from study.

Test Sites and Dates

Field tests of repellent efficacy were conducted at two field sites in the Central Valley of California chosen to represent different habitat types. Sites were also chosen based on mosquito population and habitat evaluation by CLBR staff. The sites differed in vegetative structure, water bodies and the composition and relative abundance of foraging mosquito species present (Tables 3, 7). Site 1 is hedgerow and forest remnant beside irrigated fields near an irrigation ditch, while Site 2 is mature floodplain forest surrounding some marshy areas with standing water.

Study Table 3. Field sites of ThermaCELL® efficacy study.

Site no.	Date	County	Habitat type
1	11 and 13 September 2013	Placer	Hedgerow beside irrigated fields near irrigation ditch
2	18 and 20 September 2013	Glenn	Tall floodplain oak forest

Environmental Conditions

Ambient temperature (°C), relative humidity, light intensity (lux), wind speed (MPH) were measured at approximately 1-hr intervals. Note that the hedgerow and forest vegetation slowed the wind, thus allowing the allethrin vapor to remain on-site and distribute more evenly in the air column.

Layout of stations for assays of repellency and mortality

Field efficacy was tested in two different habitats (Table 2), with 4-hour and 12-hour mats tested on separate days at each habitat site. In each habitat, treated and control mats were tested simultaneously across multiple stations in a non-blinded Latin square design. Stations were arrayed approximately perpendicular to the prevailing wind direction and a minimum of 25 meters (82 feet) from one another within the habitat at microsites (areas the same size as the stations) considered likely to provide sufficient mosquito activity throughout the testing period. At each site, 6 stations were established on the first test day at the site, during which the 12-hour mats were tested. On the second test day at each site, 4-hour mats were tested at 4 to 6 of the previously established stations. Site maps with station positions and scale distances are provided for each habitat in Appendix 5.

Each station consisted of 2 traps, 8 poles for hanging laboratory-reared mosquitoes in net cages, and an emitter (a standard, commercially available ThermaCell® device operated via label instructions to simulate consumer use). For efficiency, each station was approached throughout the day by researchers from a single access point on its perimeter. This access point was positioned in the center of the downwind face of the square defining the station area given the wind direction at that station at the beginning of the day. From the perspective of standing at this access point, bags of caged mosquitoes were arranged on poles given near and far position numbers 1, 2, 3 and 4 clockwise from the lower left quadrant. Bags were 3.25 by 2 3/8 inch (83 mm x 60 mm) fine-mesh nylon. Traps were initially positioned at 45 degrees off the axis of initial wind direction and in the near left and right quadrants. Traps were moved by the Study Director as needed at the beginning of intervals in response to shifts in wind direction to maintain traps downwind of the emitters while the grid of near and far poles were maintained constant, providing sampling coverage of the entire station area throughout the day. Resulting trap positions are documented on the datasheets entitled 'Trapped Mosquito Counts' (Appendix 3).

As per Protocol (Appendix 1), poles and traps were placed roughly 45 degrees off the axis of dominant air movement and 4 feet (122 cm) and 8.5 feet (259 cm) from the emitter for near and far samples, respectively. The traps used were Megacatch® traps (see Study Protocol, Appendix 1). Traps lured mosquitoes with a combination of light and carbon dioxide emissions. Traps were operated at identical settings. Individual traps remained at a given station throughout a test day, with exact trap position determined by both air movement and shifting patches of sunlight that might affect mosquito distribution within the station area. In general, they were kept downwind of the emitter.

Each emitter was centered in a station's area about 30 inches (76 cm) above the ground. At the beginning of a test day, each Test Material and control mat was placed on an emitter, then the emitters and their mats were assigned initial station, and treated emitters given about 30 minutes to warm up and charge the treated area with repellent. Emitters were uniquely identified, and individual pads stayed installed on the emitter for the duration of the test day. Emitters were not re-used after completion of a test day. Butane cartridges for each emitter were changed at approximately 3-hour intervals to avoid device shutdown due to lack of fuel.

Emitters were cycled systematically through the trap stations. Emitter units were cycled by moving them between stations on foot where stations were closer together (82 – 101 feet/25 to 30 meters) and by mountain bike where further apart. In most cases, emitters were moved in rotation in the sequence of station numbers 6 ->1 -> 2 -> 3 -> 4 ->5 -> 6 for tests of the 12-hour (long-life) mats and 4 -> 1 -> 2 -> 3 -> 4 for the 4-hour mats. Each emitter move and exchange

took some time to complete, closely tracking the time allotment described as 'approximately 30-50 minutes' within the Study Protocol. In some cases following the first exposure interval, some stations had shorter total exposure times for both mortality and repellency to keep total combined exposure and rotation times close to or within a one-hour period. Control and treated conditions followed one another in the rotation. At least ten minutes 'charge time' was allowed at a station for volatilized repellent to dissipate (for intervals where a control emitter replaced a treated one) or to build up (for intervals where a treated emitter replaced a control one) within the station area. Within a rotation for 4-hour mat test days, there were two treated and two control mats. Within a rotation for 12-hour mat test days, there were three treated and three untreated mats.

Carbon dioxide baited traps captured wild mosquitoes lured into the area of a given station during the exposure period, while laboratory-reared mosquitoes were placed in small mesh bags (cages) on the poles at a height of about 6 inches (15 cm). Exposure durations ranged from 20 to 61 minutes. At the end of an exposure period, trapped wild mosquitoes were collected, counted, and identified, while caged laboratory-reared mosquitoes were removed from exposure, assayed for apparent morbidity, and transferred to coolers. Caged mosquitoes were assayed again after about 24 hours to determine 24-hour morbidity and mortality. The data collected is summarized below in Table 2 from the study.

Study Table 2. Summary of Data Records, Study SCI005

Measure recorded	Title of Data Sheet	Appendix Reference	Study Objective/ Protocol Compliance
Trapped Mosquito numbers, total and by sp.	TRAPPED MOSQUITO COUNTS	Appendix 3	Repellency & ambient wild mosquito foraging intensity
Trap Position	TRAPPED MOSQUITO COUNTS	Appendix 3	Position of traps within a given station during a given exposure interval
Trap CO2 Level	TRAPPED MOSQUITO COUNTS	Appendix 3	Levels of Carbon Dioxide released by a given trap during a given interval, 1 to 5 scale
Field ambient air temperature, relative humidity, light intensity, wind speed, cloud cover	Field Environmental Conditions	Appendix 5	Overall site (habitat) conditions relevant to wild mosquito activity and caged mosquito viability for a given site on a given day; wind speed also for compliance with maximum allowed for repellent device functional testing
Time (clock time) bags ('cages') of laboratory-reared mosquitoes were placed at stations during a given exposure interval	Station Loading Times for Bags of Laboratory-Reared Mosquitoes, Master Time Data Entry Sheet	Appendix 5	Compliance with Protocol Page 8 Section 9 first paragraph, sentences 1-3

Table 2 continued...

Measure recorded	Title of Data Sheet	Appendix Reference	Study Objective/ Protocol Compliance
Morbidity and/or mortality of laboratory-reared mosquitoes within 1 hour and at about 24 hours after exposure	MORBIDITY OR MORTALITY COUNT	Appendix 4; time records data-entered in Master Time Data Entry Sheet found in Appendix 5	'knockdown' of laboratory-reared mosquitoes as expressed by observed morbidity within one hour of the end of exposure as well as observed morbidity and mortality observed the day after exposure
Pre-charge initiation time for each station at the beginning of a given test day	Research Notes Note to File, Pre-charge Initiation time for each Station, Master Time Data Entry Sheet	Appendix 5, in chronological sequence with Station Characterization Information data records	Compliance with Protocol Page 8 Section 9 first paragraph first sentence
Treatment condition of each station during a given interval	Station Characterization Information, Master Time Data Entry Sheet	Appendix 5	Compliance with Protocol Page 6 Section 7
Identification number of an individual mat and the emitter it was used on	Station Characterization Information, Master Time Data Entry Sheet	Appendix 5	Compliance with Protocol Page 6 Section 7
Orientation of a given station established at the beginning of a given test day	Station Characterization Information, Master Time Data Entry Sheet	Appendix 5; see also Note to File dated 11 Sep 2013, 'Physical Set up ... Stations' in Appendix 1	Compliance with Protocol Page 5 Section 6 fourth paragraph
'Time Start' = clock time an emitter was placed at a given station at the beginning of a given interval	Station Characterization Information, Master Time Data Entry Sheet	Appendix 5	Compliance with Protocol Page 8 Section 9 first paragraph, second sentence
'Time End' = clock time an emitter was removed from a given station at the end of a given interval	Station Characterization Information, Master Time Data Entry Sheet	Appendix 5	Compliance with Protocol Page 8 Section 9 first paragraph, third sentence and all Protocol references to "30-50 minutes"

Procedure continued

At the completion of the test day, each emitter was shut off, the labeled plastic carrier bag was removed from the emitter, the mat removed and wrapped in foil, then cloth (to prevent melting of the plastic carrier bag from contact with the still hot mat), then sealed in the labeled plastic carrier bag to prevent evaporation of the active ingredient from the mat. Each mat within its labeled plastic carrier bag was then placed in the insulated carrier bag for transport back to the laboratory. Once back to the laboratory, each individual mat and its foil wrapper were weighed together on a Sartorius H51 scale, weights recorded, then mat and foil wrapper placed back into the labeled plastic carrier bag for return to CLBR Test Material storage. Individual emitters were individually labeled with the CLBR identification number given to the mat used on that emitter, then returned to a locking storage cabinet in the laboratory at the letterhead address. None of the emitters were re-used.

Results

Field environmental conditions were suitable for testing. Repellency values for both Long Life (12-hours mat) and 4-hours mats averaged around 70% or greater for their intended durations (range 69-81% for the 4-hours mats, 70-77% for the Long Life mats). Repellency values were similar between traps placed either 4 or 8.5 feet from the emitter at each station, indicating that the performance data are applicable to areas of at least 225 square feet. In regards to the primary disease vector of concern, Culex mosquitoes were present at both study sites. The capture frequencies and total numbers of Culex captured under treated conditions were substantially lower than those captured under untreated conditions. In contrast, in terms of observed mortality and morbidity, despite some short-term morbidity affects, neither product consistently influenced the morbidity or mortality of caged mosquitoes.

Mosquito Species Present (Trapped) at Field Sites

Eight species of mosquitoes were trapped during the entire study (Study Table 7).

Table 7. Number of mosquitoes of each species collected in untreated control and treated conditions, during the efficacy trials at each site.

Mat type and	Site 1 (Placer)			Site 2 (Glenn)		
Mosquito Species	Total	Controls	Treated	Total	Controls	Treated
12-hour 'LL' mat:						
Anopheles franciscanus	1	1	0	1	1	0
Anopheles freeborni	800	621	179	513	390	223
Aedes melanimon	80	55	25	4789	3975	814
Aedes vexans	68	48	20	3375	2588	787
Aedes sierrensis	0	0	0	2	1	1
Aedes sticticus	1	0	1	1	0	1
Culex tarsalis	9	7	2	36	33	3
Culex erythrothorax	0	0	0	11	10	1
Total	929	732	197	8828	6998	1830
4-hour mat:						
Anopheles freeborni	242	193	49	201	141	49
Aedes melanimon	41	30	11	622	561	61
Aedes vexans	0	0	0	220	174	46
Aedes sierrensis	0	0	0	1	1	0
Culex tarsalis	0	0	0	1	1	0
Culex erythrothorax	0	0	0	27	26	1
Total	283	223	60	1069	911	157

Influence of time on test material performance

Sampling intervals were approximately 1 hr in duration. On the y-axis figure 1 shows percent repellency (blue) and mean total mosquitoes in untreated traps (red) during each exposure period. Only three of the four figures copies to this page from the study.

Figure 1

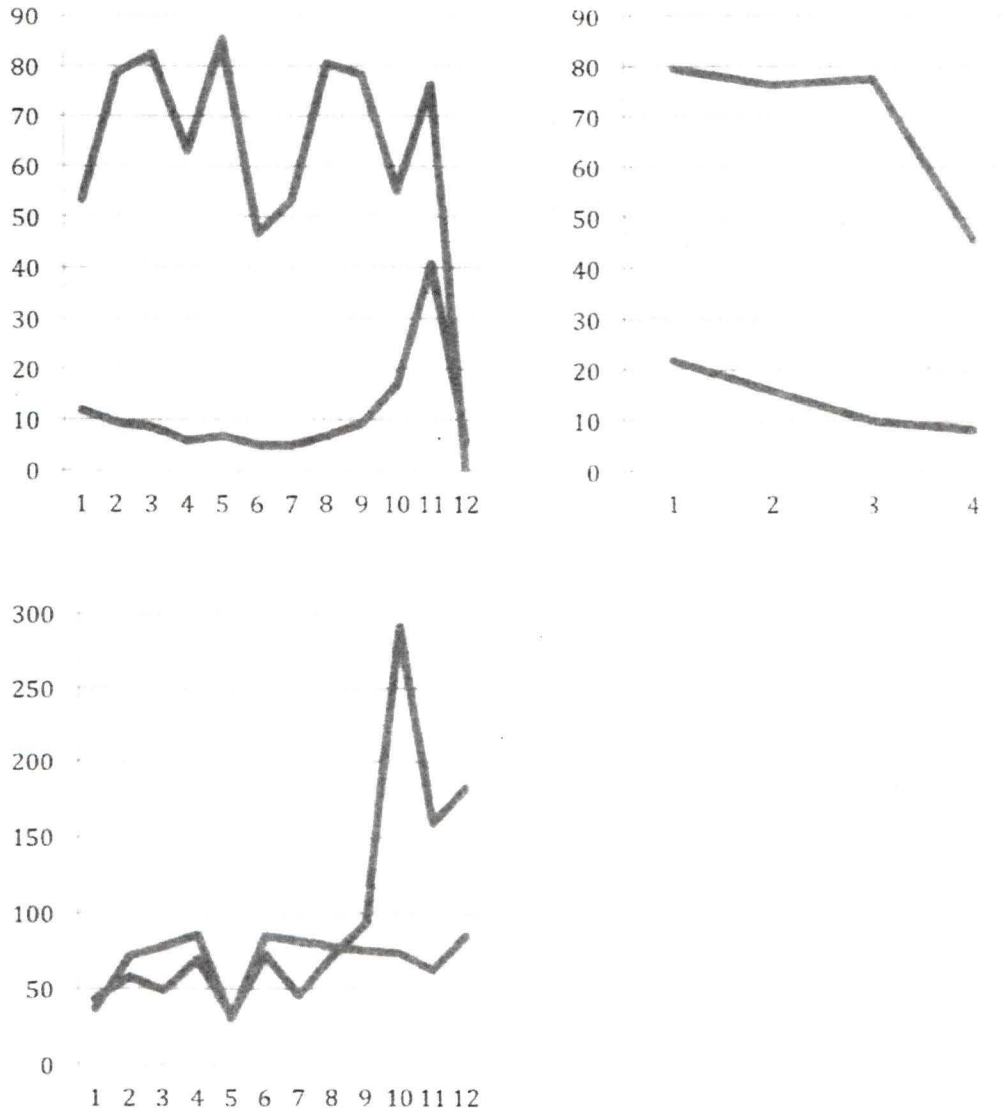

Figure 1. Percent repellency and mean numbers of mosquitoes captured in each exposure interval. Lines connect data values. Upper panels– Site 1, lower panels– Site 2. Left panels– 12-hour mat test days, right panels– 4-hour mat test days. The x-axis of each figure is interval number, not duration in hours. Hours and interval number matched except for the 12-hour mat test day at Placer (upper left panel) where 12 hours duration was reached during interval 11.

The author concluded that "percent repellency varied among exposure periods, from approximately 50-90%. Mean repellency varied only slightly between sites or days. There was no clear relationship between mosquito count and repellency. In the test of Long Life mats at Site 1 (Figure 1, upper left), exposure intervals were slightly longer than one hour on average, such that period 11 concluded 12 hours after unit ignition, while period 12 concluded 13 hours after ignition. Accordingly, high repellency continued through 12 hours, but declined thereafter. Eliminating period 12 values from the performance evaluation would slightly increase the mean repellency values presented in Table 8, above."

Repellency of wild mosquitoes:
In response, I agree with the conclusions in the paragraph above and add that the repellency response was typical for mats and coils. Variations are due to mosquito population fluctuations, local weather, and the rate of allethrin release from the mats. These graphs show that 80% or greater repellency was achieved over the duration of the study at multiple sampling time points. Lower values presented at some time points decreased the mean values to slightly less than 80%. These values are adequate for registration and amending the pending label but does not support disease vector claims as the agency has used a 90% standard for label claims of this type.

Kill and knockdown of caged mosquitoes:
'Knockdown' expressed as percent morbidity and mortality were similar between treated and untreated exposures, requiring no statistical assessments. While in the test of 4-hour mats at Site 2, 1-hr morbidity was much higher in treated exposures, later assessments then showed substantial recovery of the treated mosquitoes and no consistent differences from untreated mosquitoes. These indicates that there may be enough allethrin present to cause excito-irritant effects in host-seeking mosquitoes but the air concentrations were inadequate as an effective killing/knockdown agent. Such results are significant as they clearly show that efficacy is due to repellency instead of kill and knockdown.

Conclusion: The study is acceptable to support the proposed claims except

"34. Repel(s) [Protects(s) against mosquitoes that may (carry) (vector) (transmit) (diseases such as) (West Nile Virus) (St. Louis) (Eastern Equine) (Western equine) (LaCrosse) (Cache Valley) (or) (Venezuelan) (equine encephalitis)."

This claim is not acceptable because repellency was less than 90%, the standard EPA has used to include such claims against disease vectors. (Disease vectors were present at each site.)

Entomologist's Recommendations:

1. The submitted study is acceptable. The proposed label is acceptable except that claim #34 should be removed because repellency 90% repellency was not achieved.